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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,313	06/22/2001	Ian Tomlinson	8039/1122	9556

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EXAMINER	
STEELE, AMBER D	
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1639	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/888,313	TOMLINSON ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2008 and 03 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-68,78-86,118 and 119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-68,78-86,118 and 119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/1/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Please note: the examiner of record for the present application has changed. However, the Technology Center (TC1600) and Art Unit (AU 1639) remain the same.

Status of the Claims

2. The claim amendment received on June 3, 2008 amended claims 56, 58, 64, and 78; canceled claims 1-55, 69-77, and 87-117; and added new claims 118-119.

Claims 56-68, 78-86, and 118-119 are currently pending and under consideration.

Priority

3. The present application claims benefit of 60/246,851, filed November 8, 2000 and claims foreign priority to UK 0015443.5 filed June 23, 2000 and UK 0026099.2 filed October 25, 2000.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on February 1, 2008 is being considered by the examiner.

Regarding the Previous Office Actions

5. MPEP § 706.04 states "[f]ull faith and credit should be given to the search and action of a previous examiner unless there is a clear error in the previous action or knowledge of other prior art" (emphasis added). Therefore, the rejections made by Examiner Shibuya (after the allowance by Examiner Tran) were made in view of the rejections in a copending application by applicants (i.e. 10/008,571 which is a CIP of the present application) and in view of the references in the IDS submitted by applicants after the request for withdrawal from issue. Examiner Shibuya became aware of the rejections in the copending application due to his review of 10/008,571 for training purposes.

Invention as Claimed

6. A method for screening a first repertoire of an antibody heavy chain or antibody light chain against a second repertoire of an antibody heavy chain or antibody light chain to identify those members of the first repertoire which interact with members of the second repertoire comprising (a) arranging the first repertoire in at least one first series of continuous lines wherein each line of said first series comprises a member of said first repertoire and arranging the second repertoire in at least one second series of continuous lines wherein each line of said second series comprises a member of said second repertoire wherein the first and second repertoires form an array wherein a plurality of said first series of continuous lines intersects with a plurality of said second series of continous lines and wherein a plurality of members of the first repertoire are juxtaposed to a plurality of members of the second repertoire and (b) detecting an interaction between the antibody heavy chain or antibody light chain of the first and second repertoires thereby identifying those members of the first repertoire that interact with members of the second repertoire and variations thereof.

Withdrawn Objection

7. The objection to the specification as failing to provide proper antecedent basis for the claimed subject matter for the term "control sequence", (claim 79); the term "operatively linked", (claim 79); "naked or complexed nucleic acid", (claim 85) in the body of the specification as filed is withdrawn in view of the support shown by applicants in original claims 18 and 24 (now canceled).

New Objections

Claim Objections

8. Claims 58-59 and 60 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 56 requires a first repertoire of antibody heavy chain or antibody light chain and a second repertoire of antibody heavy chain or antibody light chain. Dependent claim 58 requires the first or second repertoire comprising dAb, dependent claim 59 requires a first repertoire comprising VH or VL, and dependent claim 60 requires a second repertoire comprising VH or VL. One of skill in the art would recognize that an antibody heavy chain or antibody light chain comprises VH (i.e. dAb) and VL, respectively. Therefore, the recitation of dAb, VH, or VL in claims 58-59 and 60 is redundant and does not further limit independent claim 56.

9. Claims 56-68, 78-86, and 118-119 are objected to because of the following informalities: independent claim 56 reads "a first repertoire of an antibody heavy chain or antibody light chain" and "a second repertoire of an antibody heavy chain or antibody light chain" which are considered to be grammatically incorrect. "[A] first repertoire of antibody heavy chains or antibody light chains" or "a first repertoire of antibody heavy chain or antibody light chain polypeptides" and "a second repertoire of antibody heavy chains or antibody light chains" or "a second repertoire of antibody heavy chain or antibody light chain polypeptides" are suggested. Please also refer to claims 58, 78, and 118-119. Appropriate correction is required.

10. Claim 78 is objected to because of the following informalities: the comma after "first" is considered a typographical error, deletion of the comma is suggested. Appropriate correction is required.

11. Claim 86 is objected to because of the following informalities: "[t]he method of claim 56, 62, 63" should read "[t]he method of claim 56, 62, or 63". Appropriate correction is required.

Withdrawn Rejections

12. The rejection of claims 56-68 and 78-86 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the claim amendments received on June 3, 2008.

13. The rejection of claims 56-68 and 78-86 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the ordinary meaning of the claims since applicants have not redefined the terms in the specification (i.e. continuous lines, juxtaposed).

14. The rejection of claims 56-68 and 78-86 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the claim amendments received on June 3, 2008.

15. The rejection of claims 56-61, 65-68, 78, 79, and 83 under 35 U.S.C. 102(b) as being anticipated by Biebuyck et al., US 6,089,853, (IDS entered 8/17/2007) is withdrawn in view of the claim amendments received on June 3, 2008.

16. The rejection of claims 56-58, 60, 62, 63, 64, 65-68, 78, and 79 under 35 U.S.C. 102(b) as being anticipated by Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS) is withdrawn in view of the claim amendments.

17. The rejection of claims 56-68 and 78-85 under 35 U.S.C. 103(a) as being unpatentable over either of Biebuyck et al., US 6,089,853, (IDS filed 8/17/2007) or Rowe et al., Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS), each take separately from the other, and each taken in view of Buechler et al., US Patent 6,057,098, (of record) is withdrawn in view of the claim amendments.

18. The rejection of claim 86 under 35 U.S.C. 103(a) as being unpatentable over either of Biebuyck et al., US 6,089,853, (IDS filed 8/17/2007) or Rowe et al., Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS), each take separately from the other, and each taken in view of Buechler et al. (US Patent 6,057,098) as applied to claims 56-68 and 78-85 above, and further in view of Bussow et al. Nucleic Acids Research 26(21): 5007-5008, 1998 is withdrawn in view of the claim amendments.

New Rejections

Claim Rejections - 35 USC § 112

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claim 118 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 118 recites the limitation "third repertoire" in lines 2 and 4. There is insufficient antecedent basis for this limitation in the claim. Changing the dependency from claim 62 to claim 63 is suggested.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 56-68, 78-86, and 118-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feldstein et al. U.S. Patent 6,192,168 filed April 9, 1999; Dower et al. U.S. Patent 5,427,908 issued June 27, 1995; and McCafferty et al. U.S. Patent 5,969,108 issued October 19, 1999.

For present claims 56-57, 62-63, 65-68, and 86, Feldstein et al. teach a microfluidic device for multianalyte interactions wherein a multimode waveguide (i.e. solid surface) is paired with a fluidic cell, flow chamber, or flow cell to perform multianalyte and multisample assays

comprising flowing a first set of reagents into multiple channels (i.e. continuous lines) wherein the first set of reagents is deposited on the waveguide, then placing another set of channels perpendicular (i.e. intersection, juxtaposed) to the first set of deposited reagents and flowing a second and/or third set of reagents through the channels (i.e. applied to single support of waveguide wherein in the upper channels are utilized for containing fluid to prohibit mixing) wherein the first, second, and/or third set of reagents can interact (please refer to the entire specification particularly the abstract; Figures 7a-7b and 8a-8b; columns 3-13; claims 1-31).

For present claims 58-61 and 64, Feldstein et al. teach antibodies and antigens (i.e. heavy and light chains; please refer to the entire specification particularly column 6, lines 37-67; column 7, lines 1-7; columns 10-12; claim 7).

However, Feldstein et al. does not teach a first repertoire of antibody heavy chains and a second repertoire of antibody light chains (i.e. antibodies utilized are multimers).

For present claims 56, 59-61, 64, 78-85, and 118-119, Dower et al. teach methods of screening single-chain polypeptides for binding comprising producing a library of antibody light chains and a library of antibody heavy chains, combining the heavy and light chains and screening for antigen binding wherein the antibody heavy and light chains are produced via phage display utilizing bacteria cells for propagation and the heavy and light chains can be expressed by the same phage or different phage (i.e. in situ production; please refer to the entire specification particularly columns 3-5, 14-15; claims 1-17).

However, Feldstein et al. nor Dower et al. teach single chain polypeptides comprising both a VH and VL (i.e. scFv) or dAb (i.e. specifically, VH and VL are taught by Dower et al.).

For present claims 56, 58-61, 78-86, and 118-119, McCafferty et al. teach methods of screening libraries of scFv and dAb for binding utilizing phage display (please refer to the entire specification particularly Figure 1; column 11; Examples 1-48).

The claims would have been obvious because the substitution of one known element (i.e. antibody; multimer taught by Feldstein et al.) for another (i.e. separate VH and VL, scFv, or dAb taught by Dower et al. and/or McCafferty et al.; utilization of scFv in sandwich assay taught by Feldstein et al.) would have yielded predictable results (i.e. VH-VL binding, antibody-antigen binding, etc.) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

23. Claims 56-68, 78-86, and 118-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS); Stevens et al. U.S. Patent 6,485,943 filed March 22, 1999; and McCafferty et al. U.S. Patent 5,969,108 issued October 19, 1999.

For present claims 56-57, 62-68, and 86, Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies and adding samples flowed through horizontal channels (first repertoire and/or second repertoire) wherein the vertical and horizontal channels are at 90° angles (please refer to entire reference particularly Figure 1; experimental section).

However, Rowe et al. does not specifically teach utilizing VH or VL in separate channels (i.e. multimer antibodies are utilized).

For present claims 59-61, Stevens et al. teach methods of making recombinant antibody subunit dimers including VH-VH and VL-VL and screening against antigen comprising providing VH and/or VL and interacting the VH and/or VL (please refer to entire specification particularly abstract; column 4, lines 44-67; column 5, lines 1-9; column 6, lines 20-41; column 7, lines 23-36; columns 9-10).

However, neither Rowe et al. nor Stevens et al. teach dAb (i.e. specifically, VH and VL are taught by Stevens et al.) or phage display.

For present claims 58-61, 78-86, and 118-119, McCafferty et al. teach methods of screening libraries of scFv and dAb for binding utilizing phage display and propagation in bacterial cells (please refer to the entire specification particularly Figure 1; column 11; Examples 1-48).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. and the dAb and phage display taught by McCafferty et al.

One having ordinary skill in the art would have been motivated to do this because Rowe et al. teach that immunosensors are easy to use, provide rapid assay times, have sensitivity comparable to ELISA, and can be utilized to study multianalyte binding (please refer to introduction and conclusion sections). In addition, Stevens et al. teach homologous dimerization of antibody subunits and altering amino acid sequences in the interfacial segments to improve yields of Fab and Fv products and studying the interactions via dimerization assays/screens (please refer to columns 4-5).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. and the dAb and phage display taught by McCafferty et al. because Rowe et al. teach utilizing immunosensors to study multianalyte interactions (e.g. VH, VL, antigen, dimmers, trimers; please refer to conclusion).

Moreover, the claims would have been obvious because the substitution of one known element (i.e. antibodies taught by Riwe et al. and Stevens et al.) for another (i.e. antibodies displayed via phage as taught by McCafferty et al.) would have yielded predictable results (i.e. VH-VL binding, antibody-antigen binding, etc.) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Therefore, the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. and the dAb and phage display taught by McCafferty et al. render the instant claims *prima facie* obvious.

Double Patenting

24. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 56-68, 78-86, and 118-119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 12, and 14-44 of copending Application No. 10/161,145. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the present invention and the invention of U.S. application 10/161,145 are drawn to methods comprising arraying a plurality of polypeptides on a support which can be single-chain or two-chain, arraying a second plurality of polypeptides/targets on a support which can be single-chain, and juxtaposing the supports so that either two-chain or three-chain polypeptides are produced.

For present claims 56-68, 78-86, and 118-119, U.S. application 10/161,145 claim immobilizing target molecules on a first support wherein the target molecules can be protein, polypeptide, amino acid, whole cell or cell extract (e.g. antigen, single-chain polypeptide, VH, VL), arraying a plurality of polypeptides on a second support wherein the polypeptides can be antibodies (e.g. VH, VL, VH-VL, VH-VH, VL-VL), juxtaposing the first and second supports wherein binding can occur (e.g. making a two-chain or three-chain polypeptide library) and phage display with propagation in bacteria (please refer to claims 1-10, 12, and 14-44).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 56-68, 78-86, and 118-119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-23 of copending Application No. 11/413,427. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 11/413,427 are drawn to methods comprising arranging a first repertoire in at least one first series of continuous lines, arranging a second repertoire in at least one second series of continuous lines forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires.

For present claims 56-68, 78-86, and 118-119, U.S. application 11/413,427 claims a method comprising arranging a first repertoire in at least one first series of continuous lines wherein the first repertoire can be VH or VL, arranging a second repertoire in at least one second series of continuous lines wherein the second repertoire can be VH or VL, forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires, optionally contacting the array with target (e.g. antigen), and allowing binding to create two- or three-chain polypeptides, dAb, phage display, etc. (please refer to clams 1 and 3-23).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

27. Claims 56-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11, 17, and 54-70 of copending Application No. 10/008,571. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as

claimed in U.S. application 10/008,571 are drawn to methods comprising arranging a first repertoire in at least one first series of continuous lines, arranging a second repertoire in at least one second series of continuous lines forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires.

For present claims 56-68, U.S. application 10/008,571 claims a method comprising arranging a first repertoire in at least one first series of continuous lines wherein the first repertoire can be VH or VL, arranging a second repertoire in at least one second series of continuous lines wherein the second repertoire can be VH or VL, forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires, optionally contacting the array with target (e.g. antigen), and allowing binding to create two- or three-chain polypeptides (please refer to claims 11, 17, and 54-70).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

October 11, 2008